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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,672	09/23/2003	Samuel I. Stupp	NANO 105 US2 (NU 22074)	1810

62249 7590 05/30/2008

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EXAMINER	
NOAKES, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
05/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,672	STUPP ET AL.	
	Examiner	Art Unit	
	SUZANNE M. NOAKES	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-15,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/07; 12/12/07; 05/05/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendments to the claims and specification in the reply filed 10 March 2008 are acknowledged. Applicants have canceled claims 1-12 and 16 and added new claims 17 and 18 which are commensurate in scope with the previously elected and examined claims 13-15. Thus, claims 13-15, 17 and 18 are pending and subject to Examination.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted 15 November 2007, 12 December 2007 and 05 May 2008 have been considered by the examiner. It is noted that the IDS from 12 December 2007 has been submitted to rectify Applicant's inadvertent omission of previously cited WIPO documents (cited on the IDS's from 16 February 2007 and 12 April 2007 – see previous Office action and see Applicants IDS letter submitted 12 December 2007). See initialed and signed PTO-1449's.

Drawings

3. The Replacement Drawings filed 07 December 2007 are accepted by the Examiner.

Withdrawal of Rejections/Objections

4. Any rejection/objection recited in the previous Office action and not explicitly restated below is hereby withdrawn.

New Rejections/Objections

Claim Rejections - 35 USC § 112 – 2nd paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 13-15, 17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are deemed indefinite because what exactly is "tissue engineered material" is not defined. Is this merely just the peptide-amphiphile composition which comprises SEQ ID NO: 1 and/or 2, or must there be something more to said composition in order to make it into a "tissue engineered material"? Is “tissue engineered material” synthetic tissue, or a composition such a gel with natural tissue cells interspersed? It is noted that said term is not defined in the specification and there is no art-defined or recognized definition. In addition, the claim and issue is further confused by the last line of claim 13: “wherein said peptide-amphiphile composition contains a peptide amphiphile composition comprising SEQ ID NO: 1 or SEQ ID NO: 2". So the peptide amphiphile composition further contains another peptide amphiphile composition?

New Rejections/Objections - Necessitated by Amendments

Claim Rejections - 35 USC § 112 – 2nd paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 13-15, 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The methods are drawn to a method of treating a patient with a tissue engineered material by administering to a site of patient in need thereof a peptide-amphiphile composition which will promote axon outgrowth of a neuron. However, not all patients can be treated by this composition, rather only those patients which will require axon outgrowth of a neuron. For instance, would administering this composition to the site of burn on a patients foot treat the patient and promote axon outgrowth of neurons? It appears that the preamble of said claims do not match the active method steps.

Claim Rejections - 35 USC § 112 – 1st paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient with tissue engineered material by administering a peptide amphiphile composition which promotes axon outgrowth of a neuron by administering a peptide amphiphile composition comprising SEQ ID NO: 1 or a mixture of SEQ ID NO: 2 *and* SEQ ID NO: 1, does not

reasonably provide enablement for the same method wherein only SEQ ID NO: 2 is used. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

It is noted the following is taught in the specification (see p. 7, lines 9-13):

> The peptide-amphiphile compositions may include amino acids in the peptide sequence which promotes cell-substrate adhesions, a first biological signal, among nerve cells like YIGSR (SEQ ID NO: 3). The peptide-amphiphile composition may include another peptide sequence, a second biological signal, which promotes axon outgrowth in cells like IKVAV (SEQ ID NO: 4).

It is noted that YIGSR (SEQ ID NO: 3) is found within the instant claimed SEQ ID NO: 2 and IKVAV (SEQ ID NO: 4) is found within the instantly claimed SEQ ID NO: 1; e.g. the following are the amino acid sequences of the instantly claimed SEQ ID NO: 1 and 2.

AAAAGGGE**IKVAV** (SEQ ID NO: 1)

AAAAGGGE**YGISR** (SEQ ID NO: 2).

Thus, given what is taught in the specification and what is known in the art, there is no expectation that a peptide amphiphile composition containing SEQ ID NO: 2 alone would be able to promote axon outgrowth of a neuron. Rather, the specification suggests that this subsequence is only capable of cell adhesion. What is required for the composition to achieve this limitation is the presence of SEQ ID NO: 1.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 13-15, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Stupp et al. (US 7,371,719 – the equivalent US Pregrant Publication 20040001893 was cited on IDS from 02/16/2007) which has a priority date of 02/15/2002.

The applied reference has two common inventors, Samuel I. Stuff and Jeffrey D. Hartgerink, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are drawn to a method of treating a patient with a tissue engineered material by administering a peptide-amphiphile composition wherein a peptide-amphiphile composition is administered to a patient wherein said peptide-amphiphile composition promotes axon outgrowth of a neuron and wherein said peptide-amphiphile composition comprises SEQ ID NO: 1 or 2 (claim 13); SEQ ID NO: 1 and 2 (claim 14) at various concentrations (claim 15); wherein said amphiphiles are

present in charge equivalent ratios, wherein the charge equivalent ratio requires to parts SEQ ID NO: 1 to 1 part SEQ ID NO: 2 (claim 18).

Stupp et al. teach peptide-amphiphile (PA) compositions which can be used for various applications and methods. It is specifically taught (see column 4, lines 34-40):

> It can also be an object of the present invention to provide peptide amphiphile compositions comprising two or more oppositely charged peptide components, each such component as can further include the same or a differing bioactive epitope sequence, for subsequent biomedical applications including without limitation either in vitro or *in vivo drug delivery, cell therapies or tissue engineering*.

Also it is taught: (see column 8, last paragraph to column 9, lines 1-16)

> In part, the present invention also provides a sol-gel system including 1) a polar or aqueous solution and/or containing of one or more of the amphiphile compounds or compositions described herein, and 2) a factor or reagent sufficient to induce assembly, agglomeration of gelation under neutral or physiological conditions. Such gelation and/or self-assembly of various PA compositions into micellular nanofibers can be achieved under substantially neutral and/or physiological pH conditions through drying, introduction of a mono- or multivalent metal ion and/or the combination of differently charged amphiphiles. The approach of using differently charged amphiphiles can also be utilized to deliver in the self assembling nanofibrous system two or more bioactive molecules, each bearing different charges and this way combining the gelation technology with the delivery of multiple biological signals. Such facile factors, as described more fully below and in several of the following examples, can extend the sol-gel system and/or methodology of this invention to a variety of medical applications. These and other aspects of the present invention can be described with reference to the PA compositions provided in Table 2, below, with further reference to FIGS. 1, 10A-B and Table 1, above

Notably, Table 2 teaches peptide amphiphile 24 which has a net overall charge of +2 and is 100% identical to the instant SEQ ID NO: 2; also taught is peptide amphiphile 25 which has a net overall charge of -1 and is 100% identical to the instant SEQ ID NO: 1. With regards to peptide amphiphiles 24 and 25, and thus instant sequences SEQ ID

NO: 2 and SEQ ID NO: 1, respectively, the YIGSR peptide sequence is found within PA 24/instant SEQ ID NO: 2 and the IKVAV peptide sequence is found within PA 25/instant SEQ ID NO: 1. Stupp et al. teach the following regarding these particular peptide sequences and peptide amphiphiles 24 and 25 (see column 9, lines 46-67).

> The peptide epitopes on molecules 22-25 demonstrate the biomedical potential of the self assembling systems described here. RGD is the well known cell adhesion ligand found in fibronectin while *IKVAV, SEQ ID NO:32, and YIGSR, SEQ ID NO:33, are laminin sequences known to interact with mammalian neurons*. *IKVAV, SEQ ID NO:34, promotes neurite outgrowth in mammalian neurons, while YIGSR, SEQ ID NO:35, plays a related role in neuronal cell-substrate adhesion*. While these and other bioactive epitope sequences can be used to effect cell adhesion, proliferation or differentiation and related outcomes, in a broader context, the PA compounds/compositions and related methods of this invention can be used in conjunction with any epitope sequence capable of cellular interaction and/or binding to a cellular membrane receptor. In particular, peptide amphiphiles 23 and 25 have a net negative charge at neutral pH, whereas PH 22 and 24 have a net positive charge. *Electrostatically driven co-assembly between PA compounds 24 and 25* as well as 23 and 22 *provide mixed nanofibers that simultaneously present two biological signals in a cellular environment*.
>
> It is further taught (see column 11, lines 46-64):
>
> Accordingly, such a system can be used in conjunction with a drug, medication or other therapeutic agent, as would be understood by those skilled in the art: *the subject drug or therapeutic agent can be provided with or introduced to an appropriate aqueous or polar medium separately or in conjunction with one or more PA compounds*. Introduction of a reagent and/or factor induces nanofiber assembly and/or gelation, incorporating such a drug/agent therein, if hydrophobic, or as bound to or sorbed on the surface thereof, if hydrophilic. Disassembly or solubilization of the nanofibrous network or gel can release or deliver the drug/agent as or where required. As would be understood by those skilled in the art made aware of this invention, a range of both hydrophobic and hydrophilic drugs/agents can be utilized herewith. In particular, with regard to the peptide epitopes thereof, hydrophilic growth factors, co-factors and/or activators can be adsorbed on, delivered with and/or released by the PA compounds/compositions of this invention.

Example 7 teaches that the peptide amphiphiles 24 and 25 from Table 2 were mixed and dissolved at concentrations of 5 mg/ml and that the mixture formed a birefringent gel. It is further noted in Example 9 that what drives the formation of the peptide-amphiphiles into said gel is the elimination of the charges, e.g. one +2 peptide amphiphile (e.g. PA 24/instant SEQ ID NO: 2) would require two molecules of PA25/SEQ ID NO: 1, which has a charge of -1, to cancel out the overall charge. Thus, one would expect that the amphiphiles were necessarily present in a 2 to 1 ratio of SEQ ID NO: 1 to SEQ ID NO: 2 (meets claims 17 and 18).

Thus, Stupp et al. teach a peptide-amphiphile composition comprising SEQ ID NO: 1 and SEQ ID NO: 2 in concentrations that are between 2 and 20 mg/ml and which are expected to be present in charge equivalent ratios (e.g. one part SEQ ID NO: 2 and two parts SEQ ID NO: 1) in order to produce a gel system which is taught can be used in tissue engineering methods which would be used to treat patients in order to promote neurite outgrowth in mammalian neurons and neuronal cell-substrate adhesion.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Suzanne M. Noakes/
Patent Examiner, Art Unit 1656
14 May 2008